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LİTERATÜR TARTIŞMASI (ÜROONKOLOJİ PROSTAT CA)

Dr. Uğur Boylu

Ümraniye Eğitim ve Araştırma Hastanesi



Platinum Priority – Prostate Cancer

Editorial by Mani Menon on pp. 7–9 of this issue

A Prospective Trial Comparing Consecutive Series of Open Retropubic and Robot-Assisted Laparoscopic Radical Prostatectomy in a Centre with a Limited Caseload

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Eur Urol, 59:1-6, 2011

- 150 ardışık prostatektomi
 - 75 açık RRP
 - 75 RARP
- Endpoints
 - Onkolojik sonuçlar
 - PSM
 - PSA
 - Perioperatif komplikasyonlar
 - Kontinans
 - Potens

Demografik

	RRP (n = 75)	RALP (n = 75)	p value
Median age, yr (IQR)	64.3 (59.1–68.0)	62.8 (58.4–67.0)	0.1479*
Median PSA level, ng/ml (IQR)	7.57 (5.1–10.4)	7.72 (5.6–12.1)	0.4059*
D'Amico risk group, no. (%)			0.2647*
Low	16 (22)	12 (16)	
Intermediate	40 (53)	48 (64)	
High	19 (25)	15 (20)	
Urinary continence**	71 of 75 (95%)	73 of 75 (97%)	0.6726†
Erectile potency††	49 of 75 (65%)	37 of 75 (49%)	0.1072†

	RRP (n = 75)	RALP (n = 75)	p value*
Mean operative time, min ± SD	253 ± 41	330 ± 54	0.0205
No. of dissected lymph nodes, median (IQR)	18 (12–23)	12 (9–17)	<0.001
Attempted NSS, no. (%)			
No	26 (35)	22 (29)	0.7204
Yes	49 (65)	53 (71)	0.6230
Monolateral	19 (25)	30 (40)	
Bilateral	30 (40)	23 (31)	

Komplikasyonlar

	RRP	RALP
Total	39 in 28 of 75 patients (37%)	31 in 30 of 75 patients (40%)
Clavien grade, no (%)	39 (100)	31 (100)
Minor	18 (46)	26 (84)
1	13 (33) PVR >100 ml (n = 4) Pressure skin redness (n = 6) Lymphocoele (n = 3)	20 (64) Pressure skin redness (n = 16) Lymphocoele (n = 4)
2	5 (13) Transfusion (n = 2) Paralytic ileus (n = 2) Perineal nerve deficit (n = 1)	6 (20) Pressure skin ulcer (n = 1) Suspected malignant hyperthermia (n = 1) Epididymitis (n = 1) Vein thrombosis (n = 1) Postoperative Addison crisis (n = 1) Femoral nerve deficit (n = 1)
Major	21 (54)	5 (16)
3a	15 (38) Retention after catheter removal (n = 4) Lymphocoele (n = 4) Anastomosis stricture (n = 7)	3 (10) Bladder tamponade (n = 1) Retention after catheter removal (n = 1) Anastomosis stricture (n = 1)
3b	6 (16) Ureteral ostium lesion (n = 2) Rectal injury (n = 1) Wound dehiscence (n = 2) Multiple pelvic abscess (n = 1)	2 (6) Ureteral injury (n = 1) Port hernia (n = 1)
4a-b/5	0	0

RRP = retropubic radical prostatectomy; RALP = robot-assisted laparoscopic prostatectomy; PVR = postvoid residual.

* Modified Clavien classification of surgical complications.

Onkolojik Sonuçlar

	RRP (n = 75)	RALP (n = 75)	p value*
Tumour stage, no. (%)			
≤pT2	56 (74)	60 (80)	0.5007
pT3	18 (24)	14 (18)	0.7080
pT4	1 (2)	1 (2)	
Gleason score, no. (%)			
6	20 (27)	15 (20)	0.4394
7	38 (51)	48 (64)	0.5790
≥8	17 (22)	12 (16)	0.3810
Lymph node status (pN+), no. (%)	12 (16)	9 (12)	0.8108

RRP = retropubic radical prostatectomy; RALP = robot-assisted laparoscopic prostatectomy.
* Fisher exact test.

	RRP (n = 75)	RALP (n = 75)	p value*
PSM, no. (%)	24 (32)	12 (16)	0.0016
pT1	0/2 (0)	0/0 (0)	–
pT2	13 of 54 (24.1)	5 of 60 (8.3)	0.0107
pT2a	1 of 8 (12.5)	0 of 8 (0)	
pT2b	1 of 4 (25)	0 of 0 (0)	
pT2c	11 of 42 (26.2)	5 of 52 (9.6)	
pT3	10 of 18 (55.5)	6 of 14 (42.8)	0.2516
pT4	1 of 1 (100)	1 of 1 (100)	–
Apex	8 of 75 (10.7)	2 of 75 (2.7)	–
Side	5 of 75 (6.7)	6 of 75 (8)	–
Base	2 of 75 (2.7)	4 of 75 (5.3)	–
Apex plus base	4 of 75 (5.3)	0 of 75 (0)	–
Apex plus side	3 of 75 (4)	0 of 75 (0)	–
Base plus side	1 of 75 (1.3)	0 of 75 (0)	–
All sites	1 of 75 (1.3)	0 of 75 (0)	–
PSA-free patients**, no. (%)			
3-mo follow-up	68 of 75 (91)	66 of 75 (88)	0.7073
12-mo follow up	65 of 75 (87)	40 of 45 (89) [†]	0.3597

Kontinans & Potens

	RRP	RALP	<i>p</i> value
Continenca*, no. (%)			
Preoperatively	71 of 75 (95)	73 of 75 (97)	0.6726**
3-mo follow-up	62 of 75 (83)	71 of 75 (95)	0.0033†
12-mo follow-up	60 of 75 (80)	40 of 45 (89)††	0.0916†
Potency, no. (%)			
Preoperatively†††	49 of 75 (65)	37 of 75 (49)	0.1072**
3-mo follow-up‡	12 of 49 (25)	25 of 37 (68)	0.0085†
12-mo follow-up‡	12 of 47 (26)‡‡	12 of 22 (55)‡‡‡	0.0090†

Sonuç

- RARP, RRP'ye göre:
 - PSM oranı
 - Kontinans
 - Potensdaha iyi sonuçlar vermiştir
- Öğrenme eğrisinde bile RRP'ye eşdeğer

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Laparoscopy and Robotic Surgery

The Learning Curve of Robot-Assisted Radical Prostatectomy

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Conclusion: Surgical, oncologic, and functional outcomes of RARP improve with increasing experience. Outcomes similar to the published series by high-volume centers could be achieved after 80 to 120 RARP cases.

Robotik Radikal Prostatektomi Sonrası Biyokimyasal Nüks: 1384 Hastanın 5 Yıllık Takibi

Platinum Priority – Prostate Cancer

Editorial by Francesco Montorsi on pp. 847–848 of this issue

Biochemical Recurrence Following Robot-Assisted Radical Prostatectomy: Analysis of 1384 Patients with a Median 5-year Follow-up

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Giriş

- RP sonrası 10 yıllık BCR %35
- PSA taramasıyla:
 - *Stage ve risk migrasyonu*
 - *Erken yaşta düşük PSA ile tanı*
- Eski oranlar yeni serileri temsil etmeyebilir

Hastalar & Yöntem

- 2000-2010, >5000 hasta RARP
- 1581 hasta, 5 yıllık takip
 - *PSA'sı olmayan (n=126)*
 - *hormon veya RT (n=48)*
 - *eksik biyopsi (n=14)*
 - *adjuvan tedavi (n=9)*
- Kalan 1384 hasta dahil

Hastalar & Yöntem

- Minimum 6 kor biyopsi
- yaş, PSA, Gleason, tm vol, klinik evre, BMI
- Menon: 1182, Peabody: 399
- NS: SHIM>17
- PLND: risk>%1
 - *Genetic adaptive neural network*
 - *Tewari et al, Mol Urol, 5:163, 2001*
- extended PLND: T2b-T3, Gleason 8-10, PSA>10

Takip

- İlk yıl 3 ay, daha sonra yılda 2 kez
- Elektronik sorgulama
- Verileri eksik olanlara email
- Data işleme: klinik dışı kişiler
- BCR: American Urological Association
Localized Prostate Cancer Update Panel
report

BCR

- BCR: American Urological Association Localized Prostate Cancer Update Panel report

prostate cancer literature with regard to biochemical recurrence, the Prostate Cancer Guidelines Update Panel has recommended a standard definition for biochemical recurrence after radical prostatectomy. It is recommended that biochemical (PSA) recurrence following radical prostatectomy be defined as a serum PSA of 0.2 ng/mL or greater, with a second confirmatory level of PSA of >0.2 ng/mL. The first postoperative PSA should be obtained between 6 weeks and 3 months following therapy. The date of failure should be defined as the date of the first detectable PSA level once this value has been confirmed. The Panel recognizes that higher levels of PSA have a greater specificity for disease

Cookson et al, J Urol, 2007, 177:540

Klinik ve Patolojik Özellikler

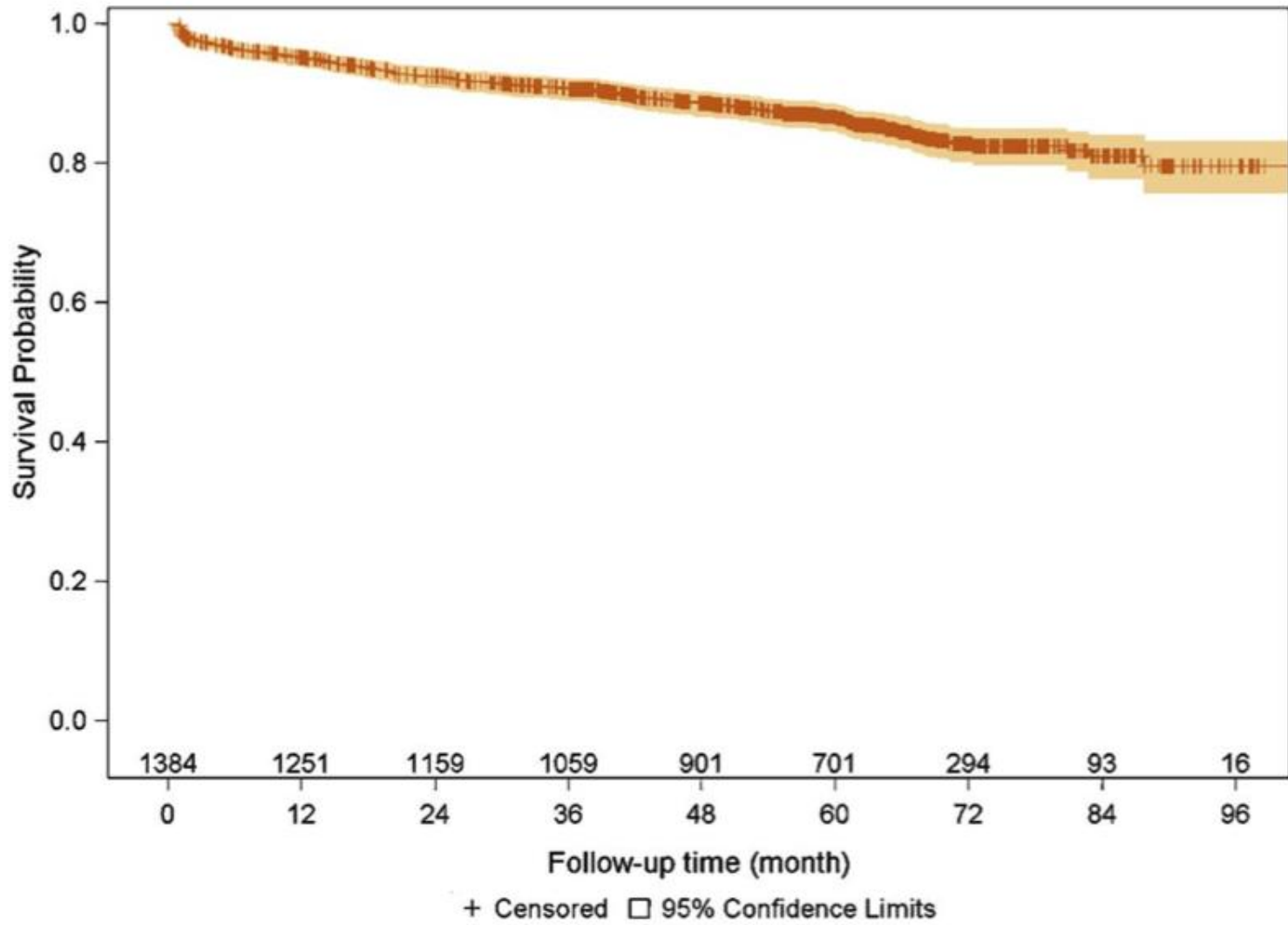
Characteristics		
Continuous	Mean (SD)	
Patient age, yr	60.0 (± 7.1)	
BMI	27.5 (± 3.6)	
Prostate weight, g	48.3 (± 20.1)	
Percent tumor volume, %	17.5 (± 13.4)	
	Median (IQR)	
Preoperative PSA, ng/ml	5.2 (4.2–7.1)	
Follow-up, mo	60.2 (37.2–69.7)	
Category	n	%
Clinical stage:		
T1a–c	1017	73.5
T2a	208	15.0
T2b	56	4.0
T2c	71	5.1
T3a	27	2.0
T3b	5	0.4
Biopsy Gleason score:		
5 or 6	844	61.0
3 + 4	347	25.1
4 + 3	103	7.5
8–10	89	6.4
Missing	1	–
Perineural invasion (biopsy):		
Absent	1236	89.4
Present	146	10.6
Missing	2	–
Nerve sparing [†] :		
Partial	716	51.7
Prostatic fascia sparing ^{**}	597	43.2
Wide excision	71	5.1

Pathologic Gleason score:		
6	541	39.1
3 + 4	563	40.7
4 + 3	165	11.9
8–10	115	8.3
Pathologic stage:		
T2a	196	14.1
T2b	23	1.7
T2c	813	58.7
T3a	293	21.2
T3b–T4	59	4.3
Margins [†] :		
Negative	1036	74.9
Positive	348	25.1
Perineural invasion ^{††}		
Absent	552	39.9
Present	832	60.1
Angiolymphatic invasion ^{††} :		
Absent	1347	97.3
Present	37	2.7
Procedure year		
2001	47	3.4
2002	254	18.4
2003	303	21.9
2004	528	38.2
2005	252	18.2

Bulgular

- Median takip 5 yıl
- 189 BCR
- 13 metastatik hastalık
- 7 PCa ölüm
- 29 diğer ölüm

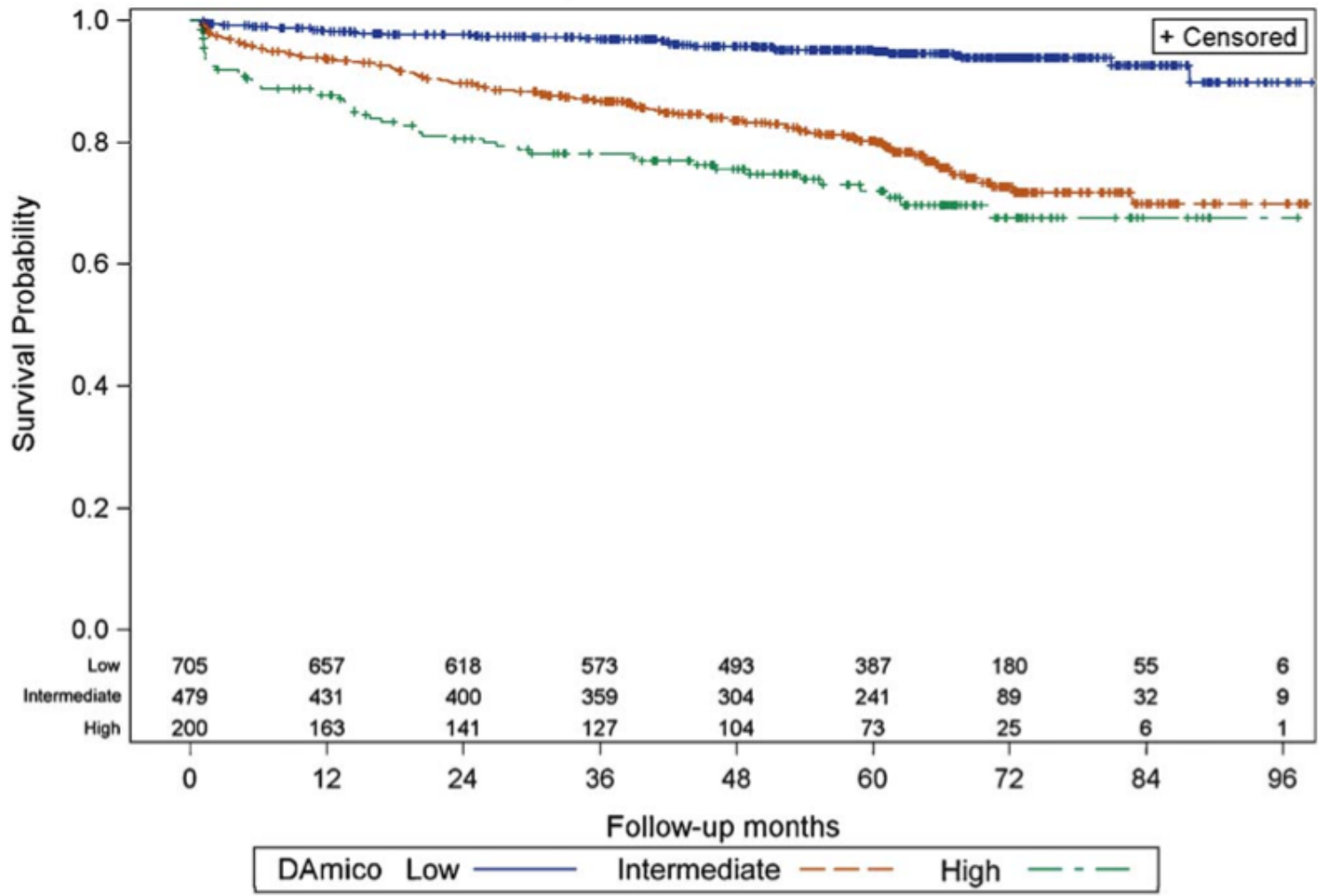
Over-All BCRFS



Overall BCRFS

- BCRFS:
 - 90.7% (95% CI, 89.0–92.1) 3 yil
 - 86.6% (95% CI, 84.6–88.4) 5 yil
 - 81.0% (95% CI, 77.6–84.0) 7 yil

BCRFS by D'Amico Risk Stratification

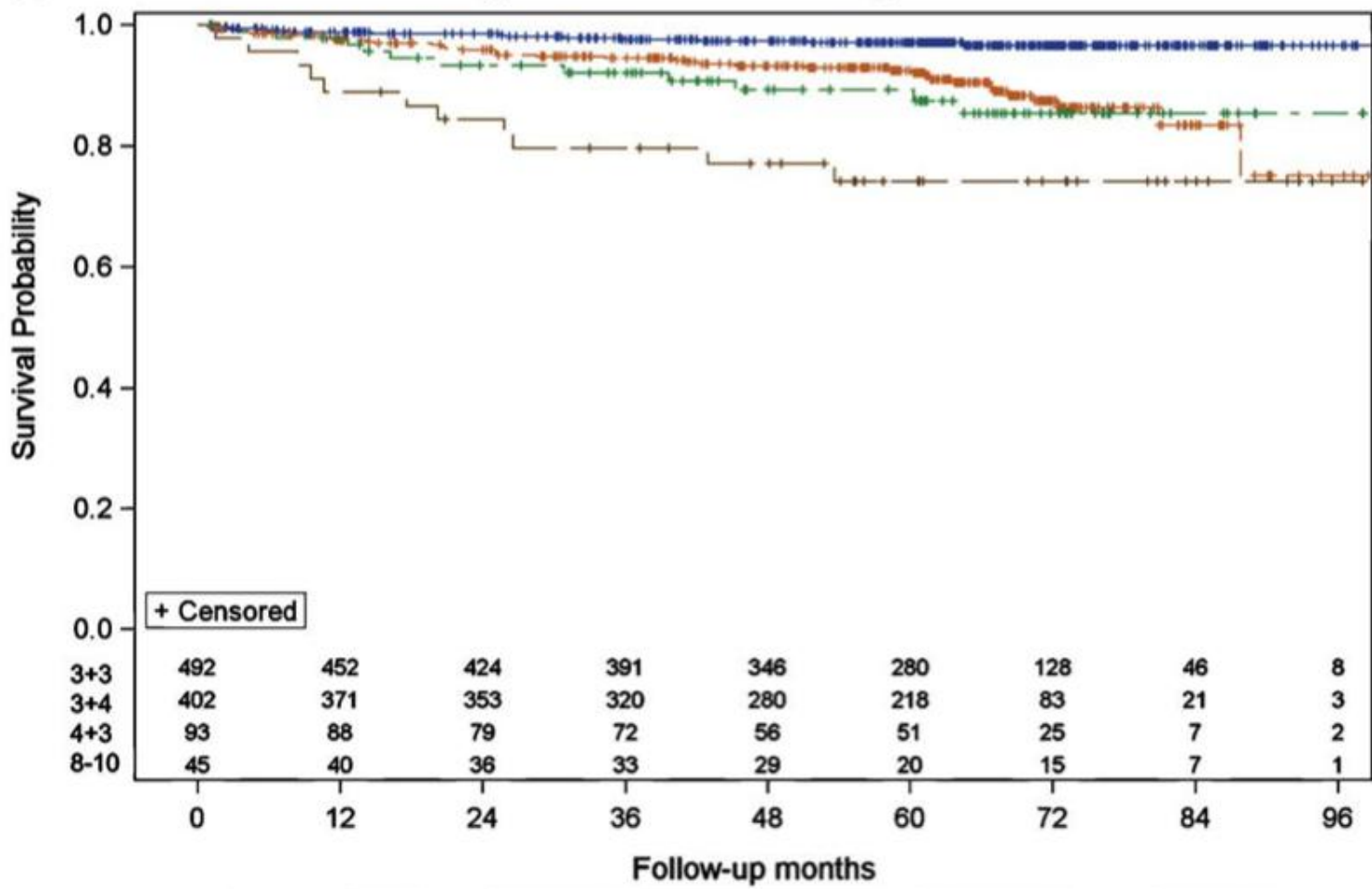


BCRFS / D' Amico

	3 yıl	5 yıl	7 yıl
düşük	%96,8	%95,1	%92,6
orta	%86,7	%80,2	%69,8
yüksek	%78,2	%72	%67,5

(a)

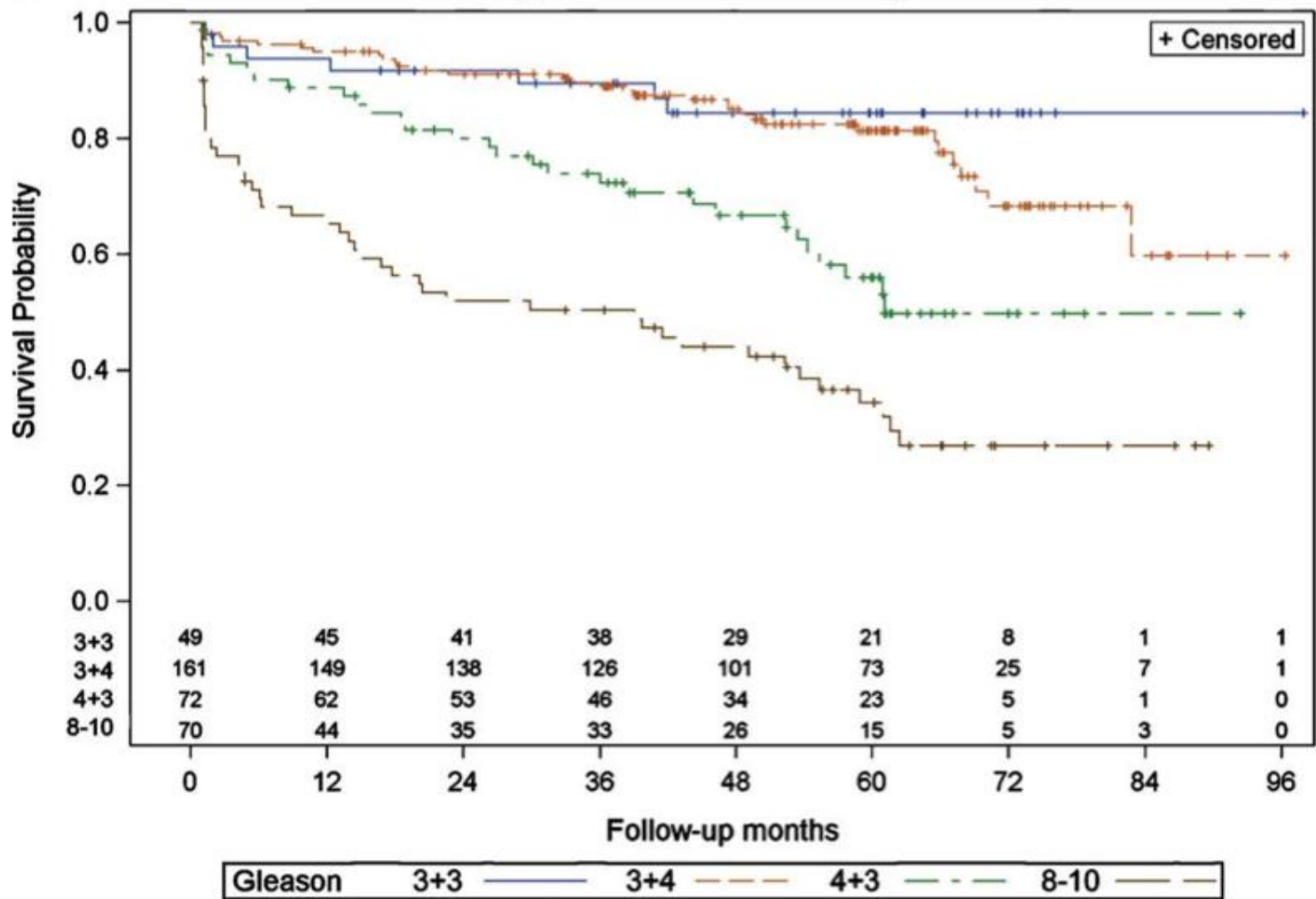
BCRFS in Organ Confined Disease by Gleason Grade



Gleason 3+3 — 3+4 - - 4+3 - - - 8-10 - - -

(b)

BCRFS in Non-Organ Confined Disease by Gleason Grade



Covariate	Univariable analysis		Multivariable analysis			
	HR (95% CI)	p value	Model 1*		Model 2*	
			HR (95% CI)	p value	HR (95% CI)	p value
Age, yr:						
<60**	1	–	1	–	1	–
≥60	1.39 (1.04–1.87)	0.0007	0.98 (0.72–1.32)	0.8792	1.20 (0.89–1.61)	0.2358
BMI:						
<25 kg/m ² **	1	–	1	–	1	–
25–30 kg/m ²	1.28 (0.83–1.96)	0.2654	1.07 (0.72–1.60)	0.7257	1.15 (0.78–1.71)	0.4846
>30 kg/m ²	1.14 (0.77–1.69)	0.5075	1.14 (0.74–1.76)	0.5600	1.21 (0.78–1.86)	0.3910
Preoperative PSA:						
≤10 ng/ml**	1	–	1	–	–	–
10.1–20.0 ng/ml	2.98 (2.03–4.38)	<0.0001	2.61 (1.76–3.86)	<0.0001	–	–
>20 ng/ml	9.17 (5.28–15.93)	<0.0001	6.16 (3.45–11.01)	<0.0001	–	–
Biopsy Gleason grade:						
5 or 6**	1	–	1	–	–	–
3 + 4	3.39 (2.36–4.87)	<0.0001	3.05 (2.11–4.43)	<0.0001	–	–
4 + 3	6.99 (4.55–10.73)	<0.0001	6.17 (3.96–9.62)	<0.0001	–	–
8–10	6.22 (3.95–9.80)	<0.0001	4.84 (3.00–7.80)	<0.0001	–	–
Clinical stage:						
T1c/T2a**	1	–	1	–	–	–
≥T2b	1.65 (1.12–2.45)	0.0118	1.42 (0.94–2.16)	0.1004	–	–
D'Amico risk group†:						
Low**	1	–	–	–	1	–
Intermediate	4.28 (2.92–6.28)	<0.0001	–	–	4.07 (2.77–5.98)	<0.0001
High	6.16 (4.02–9.45)	<0.0001	–	–	5.65 (3.62–8.83)	<0.0001
Perineural invasion†:						
Negative**	1	–	1	–	1	–
Positive	2.30 (1.60–3.32)	<0.0001	1.39 (0.94–2.07)	0.1016	1.59 (1.09–2.32)	0.0168
Procedure year††:						
2001**	1	–	1	–	1	–
>2001	0.93 (0.82–1.07)	0.3195	0.88 (0.77–1.00)	0.0569	0.88 (0.77–1.00)	0.0546

HR = hazard ratio; CI = confidence interval; BMI = body mass index; PSA = prostate-specific antigen.

* Multivariable model 2 was generated using the D'Amico risk group as a predictor, supplanting grade, stage, and PSA.

** Reference group.

† On biopsy.

†† Incorporated as a continuous value.

Covariate	Univariable analysis		Multivariable analysis	
	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value
Age, yr:				
<60*	1	–	1	–
≥60	1.44 (1.07–1.92)	0.0148	1.15 (0.85–1.55)	0.3675
Preoperative PSA:				
≤10.0 ng/ml*	1	–	1	–
10.1–20.0 ng/ml	2.98 (2.03–4.38)	<0.0001	1.64 (1.10–2.45)	0.0156
>20 ng/ml	9.17 (5.28–15.93)	<0.0001	1.95 (1.06–3.58)	0.0318
Tumor volume:				
<15%*	1	–	1	–
≥15%	2.07 (2.16–4.25)	<0.0001	1.13 (0.77–1.66)	0.5356
Pathology Gleason grade:				
6*	1	–	1	–
3 + 4	3.35 (2.06–5.46)	<0.0001	1.90 (1.13–3.19)	0.0158
4 + 3	7.01 (4.13–11.88)	<0.0001	3.05 (1.71–5.46)	0.0002
8–10	16.90 (10.24–27.88)	<0.0001	5.37 (2.99–9.65)	<0.0001
Tumor stage:				
T2*	1	–	1	–
EPE	4.60 (3.36–6.30)	<0.0001	1.78 (1.21–2.62)	0.0036
SVI/T4	11.18 (7.38–16.94)	<0.0001	2.71 (1.67–4.40)	<0.0001
Margins:				
Negative*	1	–	1	–
Positive	4.87 (3.65–6.51)	<0.0001	2.43 (1.72–3.42)	<0.0001
Perineural invasion**:				
Negative*	1	–	1	–
Positive	2.97 (2.07–4.26)	<0.0001	1.33 (0.89–1.99)	0.1584
Angiolymphatic invasion*:				
Negative*	1	–	1	–
Positive	5.54 (3.44–8.91)	<0.0001	2.15 (1.30–3.57)	0.0030
Nerve sparing†:				
Partial*	1	–	–	–
Prostatic fascia sparing††:	0.46 (0.32–0.64)	<0.0001	0.70 (0.48–1.02)	0.0633
Wide excision	1.64 (1.01–2.67)	0.0437	1.01 (0.62–1.65)	0.9653
Procedure year‡:				
2001*	1	–	1	–
>2001	0.93 (0.82–1.07)	0.3173	0.94 (0.82–1.08)	0.4035

BCR

- 9.3% (95% CI, 7.9–11.0) 3 yıl
- 13.4% (95% CI, 11.6–15.4) 5 yıl
- 17.6% (95% CI, 15.2–20.3) 7 yıl

BCR Literatür

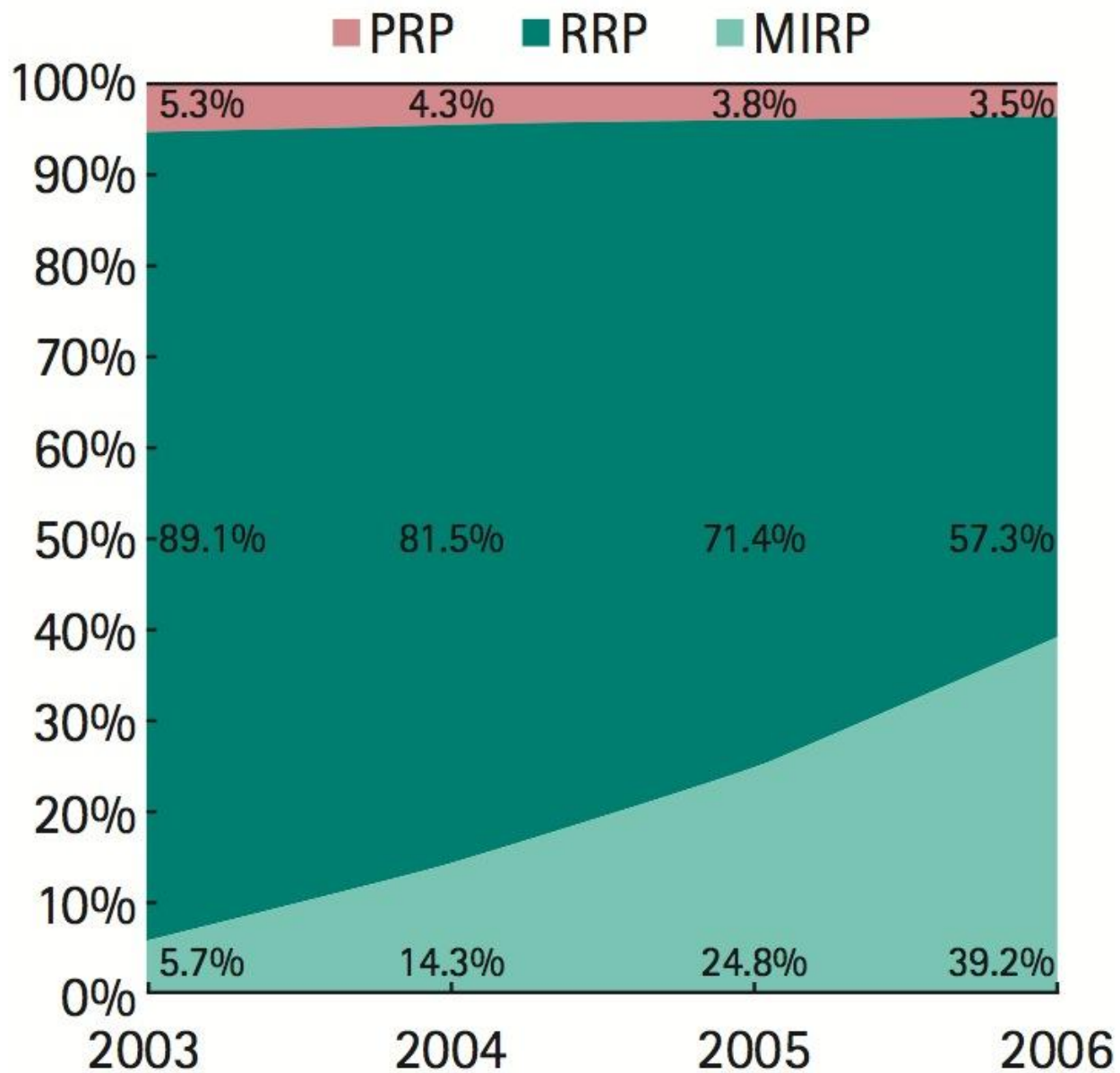
- Eastham et al
 - 1577 açık RP, 2000 - 2006
 - BCR 9%, 2 yıl median takip
- Guillonneau et al
 - 1000 LRP, 1998-2002, median takip 12 ay
 - 3 yıl progresyonsuz survival 90.5%
- Pavlovich et al
 - 508 LRP, 2000-2005
 - BCRFS 94%, median 13 ay
- Lein et al
 - 1000 LRP, 1999-2004, median 28 ay
 - 5 yıllık BCRFS: 90% pT2, 65% pT3

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- 2003 – 2006
- Veritabanları:
 - MarketScan Commercial Claims and Encounters
 - Medicare Supplemental and Coordination of Benefits
- 19.542 Prostat Ca olgusu
 - RRP
 - PRP
 - MIRP (LRP ve RARP)



	MIRP		RRP		P-value
	n	%	n	%	
Age (years)					
<55	824	20.3	2725	18.6	<0.0001
55-65	2286	56.4	7995	54.5	
65-75	875	21.6	3588	24.5	
>75	67	1.7	357	2.4	
Region					
Northeast	366	9.0	1293	8.7	<0.0001
Midwest	1489	36.8	4249	29.4	
South	1411	34.8	5280	35.8	
West	759	18.7	3761	25.5	
missing	27	-	82	-	
Charlson index					
0	1387	73.2	7248	72.7	0.1861
1-2	254	24.5	1515	25.3	
≥3	10	2.3	61	2.1	
missing	2401	-	5841	-	

TABLE 1

Demographics of the study population from 2003 to 2006

MIRP, minimally invasive radical prostatectomy; RRP, radical retropubic prostatectomy.

TABLE 2 Temporal trends in minimally invasive radical prostatectomy complications and iatrogenic injuries

	2003 (n = 287)	2004 (n = 704)	2005 (n = 1172)	2006 (n = 1889)	P-value
Mean length of stay (days)	2.1	1.9	1.9	1.7	0.004
Median length of stay (days)	2.0	1.0	1.0	1.0	-
Heterologous transfusion	0.7	2.6	2.3	0.7	0.014
Any complication within 30 days*	13.8	13.5	14.2	10.7	0.023
Cardiac	1.8	1.0	0.8	0.7	0.105
Respiratory	2.9	2.6	2.4	1.9	0.171
Vascular/clot	0.4	0.9	1.3	1.6	0.045
Wound/bleeding	0.7	0.7	1.2	1.0	0.521
Genitourinary	3.3	4.3	4.1	2.5	0.049
Miscellaneous medical	6.2	4.5	4.9	3.7	0.063
Miscellaneous surgery	3.6	4.8	3.9	2.3	0.006
Overall iatrogenic injuries within 30 days					
Intestinal injury	1.5	0.1	0.4	0.1	0.009
Re-exploration	1.8	0.6	1.0	0.7	0.211
Overall iatrogenic injuries within 6-12 months					
Rectal repair (6 months)	1.5	1.4	1.4	0.5	0.0710
Incisional hernia repair (12 months)	1.2	2.0	1.9	-	0.622
Stricture (6 months)	6.8	7.0	5.9	6.0	0.407

TABLE 3 Temporal trends in retroperitoneal radical prostatectomy complications and iatrogenic injuries

	2003 (n = 4513)	2004 (n = 4020)	2005 (n = 3375)	2006 (n = 2757)	P-value
Mean length of stay (days)	3.2	3.1	3.1	2.9	<0.001
Median length of stay (days)	3.0	3.0	3.0	3.0	-
Heterologous transfusion	9.2	9.5	9.7	6.7	0.004
Any complication within 30 days*	18.1	16.7	18.2	14.6	0.007
Cardiac	2.0	1.4	1.6	1.2	0.046
Respiratory	4.3	4.5	4.8	3.7	0.514
Vascular/clot	2.2	1.9	2.1	2.1	0.805
Wound/bleeding	2.0	1.5	1.4	1.1	0.002
Genitourinary	2.3	2.7	2.8	2.7	0.338
Miscellaneous medical	5.9	5.6	6.5	5.0	0.474
Miscellaneous surgery	4.6	4.1	4.3	3.3	0.022
Overall iatrogenic injuries within 30 days					
Intestinal injury	0.4	0.6	0.3	0.4	0.496
Re-exploration	0.1	0.1	0.2	0.1	0.762
Overall iatrogenic injuries within 6-12 months					
Rectal repair (6 months)	1.1	1.2	1.1	0.8	0.472
Incisional hernia repair (12 months)	0.9	0.8	1.3	-	0.159
Stricture (6 months)	13.1	13.1	12.4	11.9	0.186

TABLE 4 Comparison of overall complications and overall iatrogenic injury rates between radical (RRP) and minimally invasive (MIRP) radical prostatectomy

	MIRP (n = 4052)		RRP (n = 14665)		P-value
Mean length of stay (days)	1.8		3.1		<0.001
Median length of stay (days)	1		3		-
	n	%	n	%	
Transfusion	60	1.5	1309	8.9%	<0.001
Any complication within 30 days*	472	12.5	2334	17.1	<0.001
Cardiac	33	0.9	217	1.6	0.001
Respiratory	85	2.3	598	4.4	<0.001
Vascular/clot	49	1.3	280	2.1	0.003
Wound/bleeding	37	1.0	211	1.5	0.009
Genitourinary	127	3.4	357	2.6	0.013
Miscellaneous medical	166	4.4	792	5.8	<0.001
Miscellaneous surgery	126	3.3	566	4.1	0.024
All iatrogenic injuries within 30 days					
Intestinal injury	11	0.3	59	0.4	0.226
Re-exploration	31	0.8	15	0.1	<0.001
All iatrogenic injuries within 6–12 months					
Rectal repair (6 months)	30	1.1	126	1.1	0.976
Incisional hernia repair (12 months)	30	1.8	85	1.0	0.002
Stricture (6 months)	170	6.3	1466	12.8	<0.001
Cystography within 30 days	1352	35.7	1244	9.1	<0.001

Sonuç

- MIRP vs. RRP
 - Azalmış komplikasyon oranları
 - Daha az kan transfüzyonu
 - Kısa hastanede kalış